REMARKS

Claims 1-3, 8, 10, 11, and 59 have been amended. Claim 55 has been canceled without prejudice or disclaimer. Claims 1-8, 10, 11, 48, and 57-59 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 16, lines 9-22; page 17, line 35 to page 18, line 2; page 26, lines 19-20; page 30, lines 7-14. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Advisory Action, and in the prior Office Action mailed June 26, 2003, have been overcome by amendment or are traversed by argument below.

1. Objection to Claim 59 under 37 C.F.R. §§ 1.821-1.825

The Office Action mailed June 26, 2003 asserts that claim 59 fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 because this claim recites an amino acid sequence without making reference to the sequence using "SEQ ID NO:" and a sequence identifier.

Applicants have amended claim 59 to recite that an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence as set forth in SEQ ID NO: 2; wherein the glutamic acid residue at any of positions 15, 89, or 374 may be substituted with a glutamine residue; the valine residue at any of positions 16, 127, or 242 may be substituted with an isoleucine residue; the glutamine residue at position 30 may be substituted with a glutamic acid residue; the arginine residue at any of positions 32, 104, or 356 may be substituted with a histidine residue; the serine residue at either position 38 or 362 may be substituted with a threonine residue; the glutamine residue at position 39 may be substituted with a histidine residue; the isoleucine residue at position 44 may be substituted with a leucine residue; the alanine residue at either position 47 or 129 may be substituted with a threonine residue; the valine residue at any of positions 56, 175, or 381 may be substituted with a leucine residue; the methionine residue at either position 83 or 250 may be substituted with a leucine residue; the isoleucine residue at any of positions 96, 177, or 210 may be substituted with a valine residue; the arginine residue at either position 97 or 211 may be substituted with a glutamine residue; the tyrosine residue at position 110 may be substituted with a phenylalanine residue; the threonine residue at any of positions 112, 216, or 249 may be substituted with a serine residue; the asparagine residue at position 131 may be substituted with a glycine residue; the leucine residue at either position 155 or 246 may be

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substituted with a valine residue; the lysine residue at position 198 may be substituted with a glutamine residue; the serine residue at position 235 may be substituted with an alanine residue; the cysteine residue at either position 276 or 340 may be substituted with an alanine residue; the glutamine residue at either position 291 or 365 may be substituted with an arginine residue; the threonine residue at any of positions 301, 323, or 324 may be substituted with an alanine residue; the aspartic acid residue at position 325 may be substituted with a glutamic acid residue; the glutamine residue at either position 341 or 355 may be substituted with a lysine residue; or the leucine residue at position 370 may be substituted with an isoleucine residue. Applicants contend that because claim 59, as amended, does not recite an amino acid sequence without making reference to the sequence using "SEQ ID NO:" and a sequence identifier, the objection to this claim as failing to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 should be withdrawn.

2. Rejections of claims 1-8, 10, 11, 48, 55, and 57-59 under 35 U.S.C. § 112, first paragraph

The Office Action mailed June 26, 2003 asserts a rejection of claim 59 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that claim 59 adds new subject matter into the application because the as-filed specification did not disclose the amino acid sequence recited in this claim. The Action also states that it is apparent that Applicants did not intend or contemplate the amino acid sequence recited in claim 59 at the time the application was filed. The Action further states that nothing in the specification would lead one of ordinary skill in the art to the amino acid sequence recited in claim 59.

As described in section 1 above, Applicants have amended claim 59 to encompass a genus of nucleic acid molecules encoding conservatively-substituted variants of the polypeptide of SEQ ID NO: 2. Applicants contend that because claim 59, as amended, encompasses nucleic acid molecules encoding conservatively-substituted variants of the polypeptide of SEQ ID NO: 2, as opposed to an amino sequence that was not explicitly disclosed in the as-filed specification, amended claim 59 does not add new subject matter into the application. In addition, Applicants note that claim 3, as originally filed, recited, in part, an isolated nucleic acid molecule comprising a nucleotide sequence

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encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 with at least one conservative amino acid substitution. Applicants contend that because originally filed claim 3 recites conservatively-substituted variants of the polypeptide of SEQ ID NO: 2, and the genus of nucleic acid molecules recited in originally-filed claim 3 encompasses each and every member of the genus of nucleic acid molecules recited in amended claim 59, it is clear that Applicants contemplated the nucleic acid molecules recited in amended claim 59.

Moreover, as discussed in Applicant's response to the Office Action mailed January 2, 2003, Applicants note that the instant application teaches the nucleotide and amino acid sequences for several murine and human B7-like polypeptides (Figures 1-7); that residues in a B7-like polypeptide – such as the human B7-like polypeptide of SEQ ID NO: 2 – tolerable to either conservative or nonconservative substitution can be identified by performing sequence comparisons between that polypeptide and another related polypeptide – such as the murine B7-like ortholog of SEQ ID NO: 10 (page 35, lines 21-27); and rubrics recognized in the art for making conservative amino acid substitutions (Table I; page 32). Applicants contend that sequence comparisons between orthologs were well within the skill of one having but ordinary skill in the art, and in fact, that it was the practice of one skilled in the art to perform such sequence comparisons at the time the application was filed. Applicants note that one such example of a sequence comparison is *explicitly* provided in the specification (Figure 9), and that another example was provided in Appendix A of Applicant's response to the Office Action mailed January 2, 2003. As the instant specification provides sufficient guidance to determine the residues in the *explicitly* disclosed B7-like sequences that are tolerable to conservative substitution, Applicants contend that the specification leads one of ordinary skill in the art to the nucleic acid sequences recited in claim 59. Applicants, therefore, respectfully contend that amended claim 59 also satisfies the requirements of 35 U.S.C. § 112, first paragraph.

The Office Action mailed June 26, 2003 maintains a rejection of claims 2-8, 10, 11, 48, 55, 57, and 58 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that the specification does not provide a sufficient description of a genus of nucleic acid molecules comprising a region of the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the

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polypeptide fragment has an activity of a polypeptide of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6, or is antigenic; a region of the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 comprising a fragment of at least about 16 nucleotides; a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 with at least one modification that is a conservative amino acid substitution, an amino acid insertion, an amino acid deletion, C-terminal truncation, or N-terminal truncation, wherein the encoded polypeptide has an activity of a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6; a region of the above nucleotide sequence comprising a fragment of at least about 16 nucleotides; or a nucleotide sequence that is complementary to the nucleotide sequence of any of the above nucleic acid molecules. The Action also states that because there are two B7 proteins having several different activities, and a sequence search indicates that the disclosed B7-like sequences are not related to known B7 sequences, the specification does not provide a sufficient description of the activity that is possessed by the B7-like polypeptides encoded by the claimed nucleic acid molecules. The Action further states that because the specification does not describe what amino acids are considered essential for B7-like activity, and one of ordinary skill in the art cannot envision the detailed chemical structure of the genus of nucleic acid molecules encompassed by the claims, the specification does not meet the written description requirement for claiming this genus.

Applicants respectfully disagree with the Action's assertion that because there are two B7 proteins having several different activities, and a sequence search indicates that the disclosed B7-like sequences are not related to known B7 sequences, the specification does not provide a sufficient description of the activity that is possessed by the B7-like polypeptides encoded by the claimed nucleic acid molecules. Applicants note first that the instant specification teaches that transgenic mice expressing a murine B7-like ortholog of the human B7-like polypeptides set forth in SEQ ID NO: 2, SEQ ID NO: 4, and SEQ ID NO: 6 exhibit seminal vesicle hyperplasia (page 93, lines 7-9). Applicants also note that relationship between B7-like polypeptides and other members of the B7 family (*e.g.*, B7-1, B7-2, B7-rp1, or B7-H1) is *structural*, in that both B7-like polypeptides and other members of the B7 family possess extracellular regions containing immunoglobulin V (variable) and C (constant) domains, and therefore, that both B7-like polypeptides and other members of the B7 family are members of the immunoglobulin superfamily. Applicants respectfully disagree with the Action's suggestion that an adequate written description of the claimed invention requires that the

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as-filed specification demonstrate that the disclosed B7-like polypeptides possess an activity of one of the other members of the B7 family. Applicants note that the *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement* ("*Guidelines*") state that an adequate written description of the claimed invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Guidelines,* 66 Fed. Reg. 1099, 1105 (2001). With regard to a claim directed to a genus, the *Guidelines* specifically state that the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice, *or* reduction to drawings, *or* by disclosure of relevant, identifying characteristics (*i.e.,* structure *or* other physical *or* chemical properties, *or* by functional characteristics coupled with a known or disclosed correlation between function and structure, *or* by a combination of such identifying characteristics) sufficient to show the applicant was in possession of the claimed genus. *Guidelines,* 66 Fed. Reg. 1099, 1106 (2001) (*emphasis added*).

With regard to the Action's assertion that the specification does not provide a sufficient description of the genus of nucleic acid molecules encompassed by claim 2, Applicants note that claim 2 has been amended to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 encoding a polypeptide fragment of at least about 25 amino acid residues; a region of the nucleotide sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 comprising a fragment of at least about 16 nucleotides; or a nucleotide sequence that is complementary to either of these nucleotide sequences. Applicants contend that because the specification *explicitly* teaches the nucleotide and amino acid sequences of several human B7-like polypeptides (Figures 1-3), the specification inherently discloses fragments of the nucleotide and amino acid sequences of these B7-like polypeptides, since such fragments are merely portions of the specifically disclosed full-length human B7-like nucleotide and amino acid sequences. Applicants contend, therefore, that because claim 2 recites only fragments of the disclosed human B7-like nucleotide and amino acid sequences, one of ordinary skill in the art could readily determine the structure of molecules falling within the scope of this claim, and would recognize that Applicants were in possession of the claimed invention. Applicants, therefore, submit that amended claim 2 satisfies the written description requirement of 35 U.S.C. § 112, first

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paragraph, and respectfully request that this ground of rejection be withdrawn.

With regard to the Action's assertion that the specification does not provide a sufficient description of the genus of nucleic acid molecules encompassed by claim 3, Applicants note that claim 3 has been amended to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 having at least one conservative amino acid substitution, wherein the polypeptide having at least one conservative amino acid substitution is at least about 70 percent identical to the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6; a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 having a C- and/or N- terminal truncation, wherein the polypeptide having a C- and/or N- terminal truncation comprises at least about 25 amino acid residues; a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 having at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-terminal truncation, wherein the polypeptide having at least one modification is at least about 70 percent identical to the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 and comprises at least about 25 amino acid residues; a region of any of these nucleotide sequences comprising at least about 16 nucleotides; or a nucleotide sequence that is complementary to any of these of these nucleotide sequences. Applicants note that amended claim 3 no longer recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6; or a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.

Applicants contend first that because the specification *explicitly* teaches the amino acid sequences of several human B7-like polypeptides (Figures 1-3), the specification inherently discloses truncations of these B7-like polypeptides, since truncations are merely portions of the specifically disclosed full-length human B7-like polypeptides. In addition, as discussed above, the instant application teaches (a) the nucleotide and amino acid sequences for several murine and human B7-

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like polypeptides; (b) that conservative amino acid substitutions may be made in those portions of a human B7-like polypeptide (*e.g.*, the human B7-like polypeptide of SEQ ID NO: 2) that are not conserved among B7-like orthologs (*e.g.*, the murine B7-like ortholog of SEQ ID NO: 10); and (c) rubrics recognized in the art for making conservative amino acid substitutions. Moreover, Applicants contend that one of ordinary skill in the art would appreciate that those portions of a B7-like polypeptide that do not share identity with other B7-like orthologs would be less tolerable to conservative substitution and would likely be essential for B7-like activity.

As described above, exemplary sequence comparisons, prepared according to the teachings of the instant specification and illustrating those portions of a human B7-like polypeptide that are conserved relative to a murine B7-like ortholog, were provided by the instant application and Applicants response to the Office Action mailed January 2, 2003. Applicants contend that such sequence analyses were within the skill of one having but ordinary skill in the art at the time the instant application was filed using the teachings in the instant application and knowledge in the art, and note, in fact, that such a sequence comparison was used to identify the species encompassed by the genus defined in amended claim 59. Applicants also contend that because the specification explicitly teaches the amino acid sequences for several murine and human B7-like polypeptides and that conservative amino acid substitutions may be made in those portions of a human B7-like polypeptide that are not conserved among B7-like orthologs, the specification implicitly discloses those positions within the human B7-like polypeptide tolerable of conservative substitution – *i.e.*, the specification discloses relevant, identifying characteristics, namely, the structural properties of conservatively substituted human B7-like variants – and therefore, in accordance with the *Guidelines,* provides an adequate written description of the claimed invention. In view of the teachings in the instant application and knowledge in the art at the time the instant application was filed, Applicants contend that one of ordinary skill in the art could readily determine the structure of molecules falling within the scope of amended claim 3, and would recognize that Applicants were in possession of the claimed invention. Applicants, therefore, submit that amended claim 3 satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that this ground of rejection be withdrawn.

The Office Action mailed June 26, 2003 also maintains a rejection of claims 1-8, 10, 11, 48, 55, 57, and 58 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. The Action states that because the specification provides neither a function for the B7-like polypeptides encoded by the claimed nucleotide sequences nor sufficient guidance (*e.g.*, BLAST search or functional assay) for one skilled in the art to reasonably determine whether a nucleic acid molecule encompassed by the claims encodes a polypeptide having B7-like activity, and the biological properties of a B7-like polypeptide would not be apparent to one skilled in the art, it would require undue experimentation to identify nucleic acid molecules encoding polypeptides having B7-like activity. The Action also states that because the specification does not describe how the B7-like polypeptides encoded by the claimed sequences are similar in activity to B7 proteins, the closest related sequence to the claimed sequences is a novel protein with no similar function to B7 proteins, and seminal vesicle hyperplasia in a transgenic mouse expressing murine B7-like polypeptide (*i.e.*, SEQ ID NO: 14) is not considered a function of a B7 molecule, it is not apparent from the specification how the claimed sequences are related to B7 proteins. In addition, the Action states that the amino acid sequence of SEQ ID NO: 14 is a murine sequence that is not listed in the claims, and the specification does not provide sufficient guidance or factual evidence regarding the relationship between SEQ ID NO: 14 and SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6. With regard to claim 55, the Action states that because the use of gene therapy to correct a disease or medical condition was unpredictable at the time the application was filed, the specification does not provide sufficient guidance as to how modulating B7-like polypeptide levels correlates to a therapeutic effect in an animal, and one skilled in the art would understand that a nucleic acid cannot be used to decrease the level of a gene product in an animal, it would require undue experimentation to use the recited nucleic acid molecules in a method of modulating the levels of a B7-like polypeptide in an animal.

Applicants first address the Action's rejection of claim 55 as lacking enablement under 35 U.S.C. § 112, first paragraph. Applicants respectfully disagree with the Action's assertion that because the use of gene therapy to correct a disease or medical condition was unpredictable at the time the application was filed, the specification does not provide sufficient guidance as to how modulating B7-like polypeptide levels correlates to a therapeutic effect in an animal, and one skilled in the art would understand that a nucleic acid cannot be used to decrease the level of a gene product in an animal, it would require undue experimentation to use the recited nucleic acid molecules in a

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method of modulating the levels of a B7-like polypeptide in an animal. Nevertheless, in an effort to expedite prosecution of the pending claims to allowance, Applicants have cancelled claim 55. Applicants reserve the right to pursue claims directed to a method of modulating the levels of a B7-like polypeptide in an animal in a timely filed continuation or divisional application.

Applicants next address the Action's suggestion that the specification must establish that the claimed sequences are related to B7 proteins, demonstrate how the B7-like polypeptides encoded by the claimed sequences are similar in activity to B7 proteins, or show that the seminal vesicle hyperplasia phenotype observed in a transgenic mouse expressing murine B7-like polypeptide is a function of a B7 molecule. As described above, the relationship between B7-like polypeptides and other members of the B7 family (*e.g.*, B7-1, B7-2, B7-rp1, or B7-H1) is *structural*, in that both B7-like polypeptides and other members of the B7 family possess extracellular regions containing immunoglobulin V (variable) and C (constant) domains. As a result, both B7-like polypeptides and other members of the B7 family can be *structurally* classified as members of the immunoglobulin superfamily. Applicants respectfully disagree with the Action's suggestion that the specification must disclose that the claimed molecules exhibit the functional properties of, for example, B7-1, in order to enable the claimed invention.

Applicants contend that the test for determining whether the specification meets the enablement requirement of 35 U.S.C. § 112, first paragraph, is whether one of ordinary skill in the art could make or use the invention from the disclosures in the specification coupled with information known in the art without undue experimentation. M.P.E.P. § 2164.01. As discussed above, the instant specification teaches that transgenic mice expressing a murine B7-like ortholog exhibit seminal vesicle hyperplasia, and therefore, the instant specification provides at least a functional assay whereby one skilled in the art could reasonably determine whether a nucleic acid molecule encompassed by the claims encodes a polypeptide having B7-like activity. Specifically, Applicants contend that in view of the specification's teachings, one of ordinary skill in the art could readily determine whether a specific nucleic acid molecule encodes a polypeptide having B7-like activity by expressing the molecule in a mouse and determining whether the mouse exhibits seminal vesicle hyperplasia. Applicants also contend that, in view of the state of the art at the time the instant application was filed, the amount of experimentation required to demonstrate that a particular polypeptide exhibits specific properties in a transgenic mouse would be analogous to the amount of

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experimentation required to screen numerous hybridomas in order to identify one that produces a high affinity IgM monoclonal antibody. *In re Wands*, 858 F.2d 731, 740, 8 U.S.P.Q.2d (BNA) 1400, 1407 (Fed. Cir. 1988) (holding that it would not require undue experimentation would to obtain antibodies needed to practice the claimed invention).

Applicants also respectfully disagree with the Action's assertion that the instant situation is analogous to those presented in *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 42 U.S.P.Q.2d (BNA) 1001 (Fed. Cir. 1997) or *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 U.S.P.Q.2d (BNA) 1129 (Fed. Cir. 1999). In *Genentech, Inc.*, the Federal Circuit stated that "when there is *no* disclosure of *any* starting material or of *any* of the conditions under which a process can be carried out, undue experimentation is required [and] there is a failure to meet the enablement requirement." *Genentech, Inc.*, 108 F.3d at 1366 (*emphasis added*). As a result, the Court determined that the disclosure of a cDNA encoding human growth hormone (hGH), *absent any* disclosure regarding an enzyme and process for specifically cleaving the protein encoded by that cDNA, did not enable a claim directed to a cleavable fusion product of hGH. In *Enzo Biochem, Inc.*, the Federal Circuit stated that "[w]hile every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Enzo Biochem, Inc.*, 188 F.3d at 1374. As a result, the Court determined that the disclosure that the expression of three prokaryotic genes could be regulated using antisense technology (particularly when coupled with the inventor's own failure to regulate the expression of any eukaryotic gene or even any other prokaryotic gene using antisense technology) did not enable a claim directed to the regulation of any prokaryotic or eukaryotic gene using antisense technology. Applicants contend that in contrast to the situations presented in *Genentech, Inc.* and *Enzo Biochem, Inc.*, where the skilled artisan was impermissibly required to supply a missing portion of the invention (*e.g.*, an enzyme and process for specifically cleaving hGH in *Genentech, Inc.*), a skilled artisan can perform a sequence comparison using the *explicitly* disclosed sequences and *explicit* teachings of the instant specification (*e.g.*, suitable computer program) and identify the conservatively-substituted B7-like variants of claim 3 by mere inspection (*i.e.*, the members of this genus would be immediately and intuitively evident from the results of the sequence comparison).

Applicants also respectfully disagree with the Action's assertion that the specification does

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not provide sufficient guidance or factual evidence regarding the relationship between SEQ ID NO: 14 and SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6. As discussed above, the instant specification teaches the nucleotide and amino acid sequences for several murine and human B7-like polypeptides (Figures 1-7) and an exemplary sequence comparison of the human B7-like_h1 and murine B7-like_m1 polypeptides (Figure 9) that shows a striking conservation of amino acid sequence between these polypeptides. Applicants contend that such sequence analyses were within the skill of one having but ordinary skill in the art at the time the instant application was filed using the teachings in the instant application and knowledge in the art, and that a sequence comparison of the B7-like_m1 (SEQ ID NO: 10) and B7-like_m3 (SEQ ID NO: 14) shows that these sequences share substantial sequence identity (particularly in the N-terminal portions where the immunoglobulin domains are located). Applicants contend, therefore, that the specification does indeed provide sufficient guidance and factual evidence indicating that the instantly-disclosed murine B7-like polypeptides (*i.e.*, SEQ ID NO: 10, SEQ ID NO: 12, and SEQ ID NO: 14) are orthologs of the instantly-disclosed human B7-like polypeptides (*i.e.*, SEQ ID NO: 2, SEQ ID NO: 4, and SEQ ID NO: 6). Moreover, Applicants contend that those of ordinary skill in the art would find the results of a transgenic mouse experiment using a murine B7-like ortholog to be relevant to the human B7-like ortholog, and that those of ordinary skill in the art routinely perform such experiments to determine the function of novel polypeptides. Finally, Applicants note that the amino acid sequence of SEQ ID NO: 14 is recited in claims 1-3 as originally filed, and was withdrawn from consideration only as a consequence of the Restriction Requirement mailed May 4, 2001.

Applicants contend that, in view of the teachings in the instant application and knowledge in the art at the time the instant application was filed, the as-filed specification enables the scope of the pending claims by teaching the skilled artisan how to make and use the B7-like polypeptides without resorting to undue experimentation. Applicants, therefore, submit that the claims of the instant application satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

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3. Rejections of claims 3, 8, 10, and 55 under 35 U.S.C. § 112, second paragraph

The Office Action mailed June 26, 2003 maintains rejections of claims 3, 8, 10, and 55 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

The Action maintains a rejection of claims 8, 10, and 55 as being indefinite for reciting the term "B7-like polypeptide." The Action states that the term "B7-like polypeptide" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Applicants respectfully disagree with the Action's assertion that claims 8, 10, and 55 are indefinite for reciting the term "B7-like polypeptide." As discussed in Applicant's response to the Office Action mailed January 2, 2003, an *explicit* definition of the term "B7-like polypeptide" is provided in the specification at page 16, lines 29-32, which Applicants contend controls the interpretation of this term as it is used in the claims. Applicants contend, for example, that it would be apparent to one of ordinary skill in the art that a polypeptide comprising the amino acid sequence of any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 is a B7-like polypeptide. Applicants further contend that it would be apparent to one of ordinary skill in the art that a polypeptide variant of any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 is a CHL polypeptide.

Nevertheless, in order to expedite prosecution of the pending claims to allowance, and in Applicants' view because it will have no substantive effect in the proper scope of the pending claims, Applicants have amended claim 8 to recite a process of producing a polypeptide encoded by the nucleic acid molecule of any of Claims 1, 2, or 3, and have amended claim 10 to recite that the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native B7-like gene operatively linked to the nucleic acid molecule. Applicants note that an *explicit* definition of the term "B7-like gene" is provided in the specification at page 16, lines 9-22. In addition, Applicants have canceled claim 55, rendering the rejection with regard to this claim moot. Applicants contend, therefore, that amended claims 8 and 10 are not indefinite, and respectfully request that this ground of rejection be withdrawn.

The Action also maintains a rejection of claim 3 as lacking sufficient antecedent basis for the phrase "the encoded polypeptide."

Applicants respectfully disagree with the Action's assertion that claim 3 lacked sufficient

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antecedent basis for the phrase "the encoded polypeptide." However, Applicants note that claim 3, as amended, no longer recites the phrase "the encoded polypeptide," thereby rendering this ground of rejection moot.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment, and request that the Examiner withdraw all rejections made on this basis.

4. Rejections of claims 1-3 under 35 U.S.C. § 102

The Office Action mailed June 26, 2003 maintains a rejection of claims 1-3 under 35 U.S.C. § 102(a), as being anticipated by Marra *et al.* (The Washington University-NCI Mouse EST project, seq_name: gb_est82:BF040046, July 2, 1999; GenBank Accession No. AI790785), contending that Marra *et al.* disclose an EST sequence that is complementary to the nucleotide sequences of SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5, and that is antigenic when administered to an animal. The Examiner suggests that this rejection can be overcome by amending claims 1-3 to replace the phrase "complementary to" with the phrase "the full complement of."

Applicants respectfully disagree with the Action's assertion that Marra *et al.* disclose an EST sequence that is complementary to the nucleotide sequences of SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5. As discussed in Applicant's response to the Office Action mailed January 2, 2003, the claimed nucleotide sequences (1146-1158 nucleotides) share no more than 274-286 bp of overlapping sequence with the nucleotide sequence disclosed by Marra *et al.* (530 nucleotides), and that in the overlapping regions, the sequences share an identity of between 69.6-72.6%. As also discussed in Applicant's response to the Office Action mailed January 2, 2003, Applicants contend that the meaning of the term "complementary" is a mold of the original, such that the sequence of nucleotides in a original is *preserved* in the complementary strand. Alberts *et al.*, *Molecular Biology of the Cell*, pp. 5-7 (Garland Publishing, Inc., 1994). Applicants contend that because the sequence of Marra *et al.* shares only 69.6-72.6% identity with less than half the length of the claimed sequences, the sequence of Marra *et al.* does *not* constitute a mold of the original, such that the sequence of nucleotides in any of the claimed sequences would be *preserved.* Applicants contend that were the Action's assertion that the nucleotide sequence disclosed by Marra *et al.* is complementary to the claimed sequences be taken to its extreme, any nucleotide sequence

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containing, for example, a dinucleotide that *itself* was complementary to the nucleotide sequence of SEQ ID NO: 1 would therefore be encompassed by the claims. Applicants contend that such a meaning, in the context of nucleic acid molecules, is contrary to the established meaning of the term "complementary" in the art (*see, e.g.*, claim 2 of U.S. Patent No. 6,440,699, issued August 27, 2002). Applicants contend, therefore, that Marra *et al.* does not anticipate amended claims 1-3, and respectfully request that this ground of rejection be withdrawn.

The Office Action mailed June 26, 2003 also maintains a rejection of claims 1-3 under 35 U.S.C. § 102(b), as being anticipated by Taudien *et al.* (GenBank Accession No. AF121782, published February 2, 1999), contending that Taudian *et al.* disclose a nucleotide sequence that is complementary to the nucleotide sequences of SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5, and that is antigenic when administered to an animal. The Examiner suggests that this rejection can be overcome by amending claims 1-3 to replace the phrase "complementary to" with the phrase "the full complement of."

Applicants respectfully disagree with the Action's assertion that Taudian *et al.* disclose nucleotide sequence that is complementary to the nucleotide sequences of SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5. As discussed in Applicant's response to the Office Action mailed January 2, 2003, the coding portions of the claimed nucleotide sequences share only 62.2-62.5% identity with the *genomic* sequence disclosed by Taudian *et al.* (142,742 nucleotides). As also discussed in Applicant's response to the Office Action mailed January 2, 2003, Applicants contend that the meaning of the term "complementary" is a mold of the original, such that the sequence of nucleotides in a original is *preserved* in the complementary strand. Alberts *et al.*, *Molecular Biology of the Cell*, pp. 5-7 (Garland Publishing, Inc., 1994). Applicants contend that because the sequence of Taudian *et al.* shares only 62.2-62.5% identity with coding portions of the claimed sequences, the sequence of Taudian *et al.* does *not* constitute a mold of the original, such that the sequence of nucleotides in any of the claimed sequences would be *preserved.* Applicants contend that were the Action's assertion that the nucleotide sequence disclosed by Taudian *et al.* is complementary to the claimed sequences be taken to its extreme, any nucleotide sequence containing, for example, a dinucleotide that *itself* was complementary to the nucleotide sequence of SEQ ID NO: 1 would therefore be encompassed by the claims. Applicants contend that such a meaning, in the context of nucleic acid molecules, is contrary to the established meaning of the term "complementary" in the art

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(*see, e.g.*, claim 2 of U.S. Patent No. 6,440,699, issued August 27, 2002). Applicants contend, therefore, that Taudian *et al.* does not anticipate amended claims 1-3, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment, and request that the Examiner withdraw all rejections made on this basis.

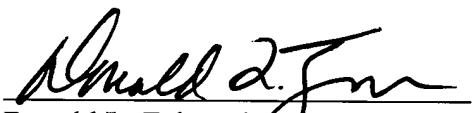
CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Whiteman believes it to be helpful, he is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: October 27, 2003

By: 
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